REMARKS

Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claim 28 is requested to be cancelled.

Claims 1-4, 8-9, 24-26, 29-31, and 42 are currently being amended.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1-4, 8-9, 24-26, 29-31, and 42 are now pending in this application.

I. OBJECTIONS

Applicants respond as follows to the several objections. See Office Action, pages 3-4.

A. Abstract

The Office asserts that two version of the abstract were filed on the same date. Office Action, page 3.

Applicants request clarification or withdrawal of this objection. A single abstract was filed on May 24, 2006, on page 50 of the specification. Applicants intended the abstract on page 50 of the specification to be the abstract of the present application.

Applicants note that the Office's Patent Application Information Retrieval (PAIR) system lists as "Abstract" the front page of publication WO 2006/045827 (corresponding to the international application of which the present application is the national phase). Applicants do not intend the front page of publication WO 2006/045827 to be the abstract of the present application.

B. Drawings

To obviate the objections, Applicants have submitted suitable corrected drawings for Figures 1, 5, and 8-10.

C. Specification

Applicants have amended the specification to remove potential hyperlinks. Applicants have revised the citations to eliminate http:// such that the text would not be interpreted as a valid HTML code to generate a live web link on the USPTO web site. See M.P.E.P. § 608.01.VII. This amendment obviates the objection.

D. Claims

To obviate the objections, Applicants have amended the objectionable claims to include an article and have amended claims 24-25 as suggested by the Office.

II. SECTION 101 REJECTION

The Office rejected claims 2-4, 28-31, and 42 under 35 U.S.C. § 101 as non-statutory because the subject matter thereof allegedly "are likely to occur in nature". The Office suggested amending the claims to recite "isolated" or "recombinant". Office Action, page 4, lines 12-14.

This rejection has been obviated by amendment for claims 2, 4, 28-31, and 42.

Claim 2 has been amended to recite "isolated".

Claim 4 currently recites "recombinant". Claim 4 is directed to cells expressing a recombinant JAK2 V617F, which implies that the cells are genetically modified. Thus, the subject matter of claim 4 would not be found in nature.

Claim 28 has been canceled.

Claim 29 has been amended to recited "isolated". Claims 30-31 and 42 have been amended to depend from claim 29.

Thus, this ground of rejection has been obviated for each relevant claim.

Applicants traverse this rejection for claim 3, which recites a "cloning and/or viral expression vector, either plasmid or in naked DNA form". Applicants submit that such a vector would not occur in nature, whether as plasmid or as naked DNA. Accordingly, Applicants request withdrawal of this ground of rejection.

III. SECTION 102 REJECTION

I think that it is acceptable to delete claim 28 which is considered overly broad by the Examiner. Nonetheless, claim 29 which specifies the structure and sequence of the siRNA should be maintained as it is clearly commensurate with the scope of the invention.

IV. SECTION 112 REJECTION (INDEFINITENESS)

The claims stand rejected as indefinite under 35 U.S.C. § 112, second paragraph, for various grounds. Applicants request that the Office withdraw this ground of rejection in view of the amendments and arguments below.

A. Claims 1-2

Claims 1-2 have been amended to identify the particular mutation "V617F" and the particular sequence "SEQ ID NO 1".

B. Claim 3

Claim 3 has been amended to delete "efficient".

C. Claims 8-9

Claims 8-9 have been amended to recite "a probe or primer".

Regarding the recitation "position 1849" in claim 8, the specification explains the location and nature of the mutations in SEQ ID NO 3 and SEQ ID NO 4. In the following quoted passage, the specification lists SEQ ID No 3 with the nucleotide at position 1849 specifically designated, and states that the "underlined sequence . . . [is] SEQ ID No 4" (see specification, page 13, lines 1-13):

> particularly, the invention pertains to an isolated nucleic acid having a sequence of at least 10, 12, 15, 20, 30, 40 or 50 consecutive nucleotides (e.g. 10 to 30 nucleotides or 10 to 25 nucleotides) of exon 12 or of the sequence SEQ ID N° 3 or N°4 below and including the mutated t^{1849} nucleotide, of 10 to 30 nucleotides for example.

SEQ ID N°3

ctcatatgaaccaaatggtgtttcacaaaatcagaaatgaagatttgatatttaatgaaagcctggccaaggcactttacaaag
attttaaaggcgtacgaagagaagtaggagactacggtcaactgcatgaaacagaagttctttaaaagttctggataaagcac
acagaaactattcagagtctttcttgaagcagcaagtatgatgagcaagctttctcacaagcatttggttttaaattatggagtatg
tt[1849]tctgtggagacgagaatattctggttcaggagtttgtaaaattggatcactagatacatatctgaaaaagaatcaaaaatt
gtataaatatattatggaaacttgaagttgctaaacagttggcatgggccatgcatttctagaagaaaacaccctattcatgggga
atgtatgtgccaaaaatattctgcttatcagagaagaagacaggaagacaggaaatcctcctttcatcaaacttagtgatcctgg
cattagtattacagttttgccaaaggacattcttcaggag

The underlined sequence designates an example of upstream or downstream areas allowing the design of probes or primers specific to the mutation at position 1849 (SEQ ID N° 4).

In the quoted passage, the specification clearly refers to "the mutated t^{1849} nucleotide" in SEQ ID No 3 or 4. It is therefore evident that claims 8-9 refer to the sequences of SEQ ID No 3 and SEQ ID No 4, and that these sequences contain a mutation that is labeled as "t^{1849}".

Further, the specification explains the mutation as follows (page 6, lines 9-13):

> The invention also relates to a nucleotide sequence encoding SEQ I D No 1, preferably SEQ ID NO 2 (sequence of the human JAK2 gene with the TTC codon instead of GTC on codon 617 (g/t mutation at position 1849 hereinafter called G1849T, starting from the ATG marking the start of translation).

Accordingly, the phrase "position 1849" in claim 8 referring to SEQ ID No 3 or 4 would be fully understood by a person of ordinary skill in the art.

Moreover, there is no basis that the Office could not search the sequences of claims 8-9, given the clear explanation in the specification, as quoted and explained above.

D. Claims 24-26 and 29-31

The Office asserted that "G1849T" and "t^{1849}" are indefinite. As explained above, the specification clearly explains the phrase "G1849T mutation" as recited in claim 25 and "mutated t^{1849} nucleotide" as recited in claim 29.

Applicants have suitably amended the phrases reciting broader and narrower scope in claims 25 and 29-30 (e.g., "suffering from Vaquez polyglobulia or from any other myeloproliferative disorder" and "reducing by more than 50%, or more than 95%").

Applicants have amended claim 31 by inserting "and" as the Office suggested.

E. Improper Antecedent Usage

Applicants have suitably amended claims 3-4, 9, 26, and 29-31 in response to the rejection for indefiniteness due to improper antecedent usage (Office Action, page 10).

V. SECTION 112 REJECTION (FIRST PARAGRAPH/NON-ENABLEMENT)

Claims 1-4, 8-9, 24-26, 28-31, and 42 stand rejected under 35 U.S.C. § 112, first paragraph, as non-enabled (Office Action, pages 10-13).

Applicants have obviated this ground of rejection by amending claim 1 to a protein "having the sequence shown in SEQ ID NO 1". The Office acknowledged enablement for this scope. Office Action, page 10, lines 3-4 from bottom.

The same reasoning applies to claims 2-4, 29-31, and 42, which depend directly or indirectly from claim 1. As such, the amendment to claim 1 also obviated this ground of rejection for these claims.

Claim 8, however, does not appear to contain any offending limitations comparable to those mentioned in the Office Action in rejecting claim 1. Applicants could not find any specific reference in the Office's non-enablement rejection (Office Action, pages 10-13) regarding why claim 8 is not enabled.

The Office did not refer to any limitations of claim 8 in the Office's non-enablement rejection. Claim 8 states (as amended) "A probe or primer ~~Probes or primers~~ comprising 10 to 30 consecutive nucleotides of sequence SEQ ID NO 3 or 4 and comprising the mutated nucleotide t^{1849}." The rejection nowhere mentions a probe or primer comprising nucleotides of SEQ ID NO 3 or 4. Claim 8 does not depend from claim 1 or any other claim, so the Office's analysis regarding claim 1 and its dependent claims are not relevant to claim 8.

The same reasoning applies to claims 9 and 24-26, which depend directly or indirectly from claim 8.

Accordingly, Applicants request withdrawal of this ground of rejection.

VI. SECTION 112 REJECTION (FIRST PARAGRAPH/POSSESSION)

Claims 1-4, 8-9, 24-26, 28-30, and 42 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of written description/possession (Office Action, page 14-15).

The Office rejected claims 1, 4, and 42 due to the scope of proteins (Office Action, page 14, lines 5-7. Applicants have obviated this ground of rejection by amending claim 1 to an isolated JAK2 protein having the sequence SEQ ID NO 1.

The Office rejected claims 2-3, 8-9, 24-26, and 29 based entirely on a pronouncement of indefiniteness with no analysis. Applicants assume this rejection is based entirely on the indefiniteness rejection found elsewhere in the Office Action. Applicants believe the indefiniteness rejection has been obviated. Accordingly, Applicants have also obviated the rejection for lack of possession.

Finally, the Office rejected claims 28 and 30 for scope exceeding three representative species of siRNA in the specification. Office Action, paragraph bridging pages 14-15.

The Office stated:

> The specification teaches the structure of only three representative species of such siRNA molecules, which are capable of reducing expression of a polynucleotide encoding SEQ ID NO: 1 in a single cell type (Figs 8-9). Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being a siRNA molecule capable of reducing expression of any polynucleotide encoding SEQ ID NO: 1 in any cell. Given this lack of description of representative species encompassed by the genus of the claims, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

This statement does not satisfy the requirements for a rejection based on lack of written description, as set forth in the Manual of Patent Examining Procedure:

> **2163.04 Burden on the Examiner with Regard to the Written Description Requirement [R-6]**
>
> The inquiry into whether the description requirement is met must be determined on a case-by-case basis and is a question of fact. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. See, e.g., *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The examiner, therefore,

> must have a reasonable basis to challenge the adequacy of the written description. The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims. *Wertheim*, 541 F.2d at 263, 191 USPQ at 97.

Here, the Office has not satisfied this burden. The Office has not explained why the disclosure of three representative species of siRNA in the specification is insufficient to show possession of the full scope of the invention.

The USPTO has stated (Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112 , ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1066, 1106):

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice (see (1)(a), above), reduction to drawings (see (1)(b), above), or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.
>
> . . .
>
> What constitutes a "representative number" [of species] is an inverse function of the skill and knowledge in the art.

The specification describes the functional characteristics of the claimed siRNA and describes correlation between function and structure on page 21, line 10, to page 22, line 13.

The skill and knowledge in the art of siRNA technology is high, in that a person of ordinary skill in the art can turn to computer programs to generate suitable siRNAs for a given nucleotide sequence. The specification states that "numerous programmes are available for the design of the siRNAs of the invention" and lists six Internet sites with resources for automatically generating siRNAs given a nucleotide sequence. Specification, page 22, lines 14-37. Accordingly, fewer disclosed species are necessary to satisfy the written description requirement.

Here, the three disclosed species are sufficient to satisfy the written description requirement in view of the high skill and knowledge in the art of siRNA technology. Accordingly, Applicants request withdrawal of this ground of rejection.

VII. ANTICIPATION

The Office rejected claims 1 and 4 as anticipated over a reference (Kawamura et al., 1994) disclosing a JAK kinase and a cell expressing the kinase. The Office recognized that Kawamura discloses a JAK kinase with methionine at the position corresponding to 617 in SEQ ID NO 1 disclosed in the present specification. Office Action, page 15, lines 3-7 from bottom.

Applicants have obviated this rejection by amending claim 1 to recite "An isolated JAK2 protein (Janus kinase 2) comprising the V617F mutation-and having the sequence shown in SEQ ID NO 1."

As amended, claim 1 requires phenylalanine ("F") at the 617 position of SEQ ID NO 1, and is not anticipated by a JAK kinase with methionine at the 617 position of SEQ ID NO 1. Accordingly, this ground of rejection should be withdrawn.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741.

If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date 1-APR-2009 By _____

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